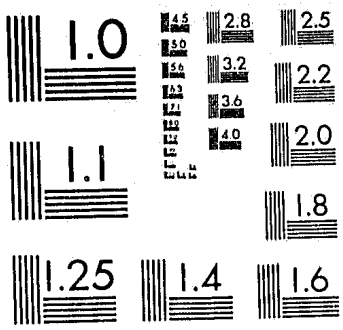

COMMONWEALTH of AUSTRALIA

PATENTS ACT 1952

APPLICATION FOR A STANDARD PATENT

I/
We RHONE-POULENC AGROCHIMIE, of

14-20 Rue Pierre Baizet,
Lyon 9e, FRANCE

hereby apply for the grant of a Standard Patent for an invention entitled:

"2, 5-DIHYDROFURAN DERIVATIVES CONTAINING TRIAZOLE OR IMIDAZOLE GROUPS, THEIR PREPARATION AND USE AS FUNGICIDES"

which is described in the accompanying ~~provisional~~ complete specification.

Details of basic application(s):—

Number	Convention Country	Date
8612098	FRANCE	22nd August 1986

LODGED AT SUB-OFFICE
20 AUG 1987
Melbourne

The address for service is care of DAVIES & COLLISON, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

Dated this 20th day of August 19 87

K. M. Rimington

To: THE COMMISSIONER OF PATENTS

.....
(a member of the firm of DAVIES & COLLISON for and on behalf of the Applicant).

Davies & Collison, Melbourne and Canberra.

PH 2726

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

DECLARATION IN SUPPORT OF CONVENTION OR NON-CONVENTION APPLICATION FOR A PATENT

In support of the Application made for a patent for an invention

Insert title of invention

entitled: 2,5-dihydrofuran derivatives containing triazole or imidazole groups, preparation process and use as fungicide

Insert full name(s) and address(es) of declarant(s) being the applicant(s) or person(s) authorized to sign on behalf of an applicant company

I/We

Patrick RANGUIS - Ingénieur au Département Propriété Industrielle
Of Rhone-Poulenc Agrochimie,
Of 14-20 Rue Pierre Baizet,
Lyon 9e,
FRANCE.

do solemnly and sincerely declare as follows :-

Cross out whichever of paragraphs 1(a) or 1(b) does not apply

1(a) relates to application made by individual(s)

1(b) relates to application made by company, insert name of applicant company.

1. (a) ~~I/we am/are the person(s) named in the application for the patent~~

or (b) I am authorized by RHONE-POULENC AGROCHIMIE, a French Body Corporate, of 14-20 Rue Pierre Baizet, Lyon 9e, France

the applicant..... for the patent to make this declaration on its ~~his/her/their~~ behalf

Cross out whichever of paragraphs 2(a) or 2(b) does not apply

2(a) relates to application made by inventor(s)

2(b) relates to application made by company(s) or person(s) who are not inventor(s), insert full name(s) and address(es) of inventors

2. (a) ~~I/we am/are the inventor(s) of the invention~~

or (b)

1). Alfred GREINER of 31 Rue des Aulnes, 69570 DARDILLY, France

2). Régis PEPIN of 27 Montée Castellane, 69140 RILLIEUX LA PAPE, France

BOTH FRENCH CITIZENS

I/We are the actual inventor(s)..... of the invention and the facts upon which the applicant..... I/We are entitled to make the application are as follows :-

State manner in which applicant(s) derive title from inventor(s)

Employee invention - Contract of employment

Alfred GREINER : 1.08.1979

Régis PEPIN : 1.03.1985, whereby the applicant would if a patent were granted or an application made by the said inventors be entitled to have the patent assigned to it.

Cross out paragraphs 3 and 4 for non-convention applications. For convention applications, insert basic country(s) followed by date(s) and basic applicant(s).

3. The basic application..... as defined by Section 141 of the Act was ~~were~~ made

in FRANCE NO. 8612098 on the 22ND AUGUST 1986
by RHONE-POULENC AGROCHIMIE
in ..... on the .....
by .....
in ..... on the .....
by .....

4 The basic application..... referred to in paragraph 3 of this Declaration was ~~were~~ the first application ..... made in a Convention country in respect of the invention the subject of the application

Insert place and date of signature

Declared at Lyon this 18 day of August 1987

Signature of declarant(s) (no attestation required)

RHONE-POULENC AGROCHIMIE
BY: Patrick RANGUIS

Note Initial all alterations

DAVIES & COLLISON MELBOURNE and CANBERRA

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(19) AUSTRALIAN PATENT OFFICE

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(71) Applicant
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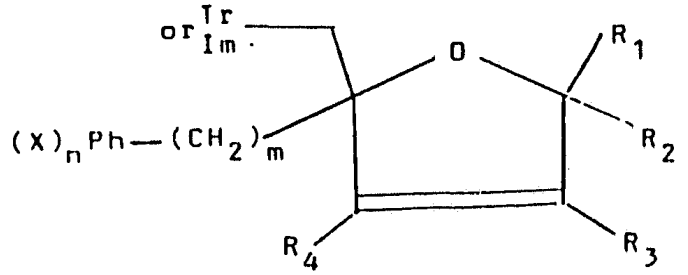
REGIS PEPIN

(74) Attorney or Agent
DAVIES & COLLISON, MELBOURNE

(54) Title
SUBSTITUTED FURYL METHYL IMIDAZOLE (OR TETRAZOLE)

(57) Claim

1. A compound of the formula:



(I)

, in which R_1, R_2, R_3 and R_4, which may be identical or different, each represents a hydrogen atom, or a lower alkyl, lower cycloalkyl, lower alkenyl, lower alkynyl or aryl radical, each such radical being optionally substituted, X represents a halogen atom, or an alkyl or alkoxy group containing from 1 to 12 carbon atoms, and optionally mono- or poly-halogenated or

X may also represent a cyano group,

n is zero or a positive integer which is less than 6, it being understood that when n is greater than 1, the substituents X may be identical or different,

Ph is an optionally substituted phenyl ring,

m = 0 or 1, and

Tr represents a 1,2,4-triazol-1-yl group and Im represents a 1,3-imidazol-1-yl group; and salts thereof and complexes thereof with metal salts.

11. A process for the preparation of a compound according to claim 1, which comprises:

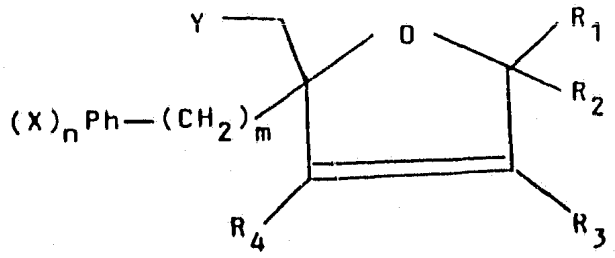
when R_3 and R_4 both represent a hydrogen atom, the hydrogenation of a compound of the formula:

$(X)_n Ph-(CH_2)_m-C(OH)\ (CH_2Hal)-C\equiv C-CR_1R_2OPr$ (IV)

in which X, n, Ph, m, R_1 and R_2 are as defined in claim 1, Pr represents a protective group, and Hal represents a halogen atom or, when one or each of R_3 and R_4 is other than a hydrogen atom, reaction of an organomagnesium compound of formula R_4MgX with a compound of formula IV and, if R_3 is other than hydrogen, addition of an alkyl halide of formula R_3X, cyclization of the compound thus obtained of the formula:

$(X)_n Ph-(CH_2)_m-C(OH)(CH_2Hal)-CR_4=CR_3-CR_1R_2-OZ$ (III)

in which R_1, R_2, R_3, R_4, X, Ph, n and m are as defined in claim 1, Hal is as hereinbefore defined, Z is a hydrogen atom or OZ is a leaving group, and the introduction of an imidazole or triazole ring into the compound thus obtained of the formula:



(II)

in which R_1, R_2, R_3, R_4, X, Ph, m and n are as defined in claim 1 and Y represents an atom or a group which can be removed by a nucleophilic substitution to introduce the imidazole or triazole ring, the groups OPr and Hal being converted if necessary, into groups OZ and Y respectively.

34. A method for the control of fungal diseases of crops at a locus which comprises the application thereto of a compound according to claim 1 or an agriculturally acceptable salt or complex thereof with a metal salt.

38. A compound of formula II, III or IV, in which X, n, m, Ph and R_1 to R_4 are as defined in claim 1 and Y, Z, Hal and Pr are as defined in claim 11.

COMMONWEALTH OF AUSTRALIA

PATENT ACT 1952

COMPLETE SPECIFICATION

(Original)

FOR OFFICE USE

Class Int. Class

Application Number:
Lodged:

Complete Specification Lodged:
Accepted:
Published:

Priority:

Related Art:

Name of Applicant: RHONE-POULENC AGROCHIMIE

Address of Applicant: 14-20 Rue Pierre Baizet,
Lyon 9e, FRANCE

NAME(S) OF INVENTOR(S): Alfred GREINER and REGIS PEPIN

Address for Service: DAVIES & COLLISON, Patent Attorneys,
1 Little Collins Street, Melbourne, 3000.

Complete Specification for the invention entitled:

"2, 5-DIHYDROFURAN DERIVATIVES CONTAINING TRIAZOLE OR IMIDAZOLE GROUPS, THEIR PREPARATION AND USE AS FUNGICIDES"

The following statement is a full description of this invention, including the best method of performing it known to us :-

The present invention relates to new compounds containing triazole or imidazole and 2,5-dihydrofuran groups, for use in plant protection or for industrial use, to their preparation and to compounds which can be used as intermediates in their preparation. The invention also relates to fungicidal compositions comprising the new compounds and to their use in methods for the control of fungal diseases of crops.

Many compounds especially fungicides, containing triazole groups are already known, in particular, from European Patent No. 151,084.

The present invention seeks to provide compounds which have improved properties in the treatment of fungal diseases, especially of cereals, and also to provide compounds which also have an improved spectrum of use against fungal diseases, especially of cereals, of grape vines and vegetable crops.

The present invention provides compounds of formula I (formula I and other formulae referred to hereinafter are depicted at the end of the description) in which: R_1, R_2, R_3 and R_4, which may be identical or different, each represents a hydrogen atom, or a lower alkyl, lower cycloalkyl, lower alkenyl (preferably allyl), lower alkynyl (preferably propargyl) or aryl (preferably phenyl) radical, each such radical being optionally substituted, for example, by one or more atoms or radicals such as halogen atoms, lower alkoxy, aryloxy (preferably phenoxy), aryl (preferably phenyl), lower alkyl, lower

haloalkyl (preferably trifluoromethyl), lower haloalkoxy (preferably trifluoromethoxy) or hydroxy radicals,

X represents a halogen atom, preferably fluorine, bromine or chlorine, or an alkyl or alkoxy group containing from 1 to 12 carbon atoms, preferably from 1 to 4 carbon atoms and optionally mono- or poly-halogenated (preferably a CF_3 group) or X may also represent a cyano group,

n is zero or a positive integer which is less than 6, it being understood that when n is greater than 1, the substituents X may be identical or different,

Ph is an optionally substituted phenyl ring,

m = 0 or 1, preferably 0, and

Tr represents a 1,2,4-triazol-1-yl group and Im represents a 1,3-imidazol-1-yl group, and salts thereof and metal complexes thereof. The salts and metal complexes are preferably agriculturally acceptable and include hydrochlorides, sulphates, oxalates, nitrates or alkyl- or arylsulphonates; metal complexes include the addition complexes of the compounds of formula I with metal salts, and especially iron, chromium, copper, manganese, zinc, cobalt, tin, magnesium and aluminium salts.

By way of example, the complexes with zinc may be obtained by reacting the compound of formula I with zinc chloride.

In this specification and the accompanying claims it is to be understood that the adjective lower, when it qualifies an organic radical, means that the radical

contains not more than six carbon atoms; organic radicals may be straight-chained or branched.

The compounds of formula I and certain compounds which may be used as intermediates in their preparation may exist in isomeric forms arising from the presence of asymmetric centres in the molecule. The invention relates to the optical isomers of the compounds of formula I as well as to the racemic mixtures thereof and to the corresponding diastereoisomers. The separation of the diastereoisomers and/or the optical isomers may be carried out by methods known per se. By the expression "methods known per se" as used in this specification is meant methods heretofore used or described in the literature.

Preferred compounds of formula I for fungicidal applications are those in which X is a halogen atom, preferably chlorine, and n = 1, 2 or 3.

Also preferred are the compounds of formula I in which n = 1 or 2, and X is a halogen atom, preferably chlorine, in the ortho and/or the para position(s), especially compounds wherein n = 2 and X is a halogen atom, advvantageously chlorine, in the ortho and the para positions.

R_1 and R_2 preferably represent a hydrogen atom and advantageously:

R_3 and R_4, which may be identical or different, each represents a lower alkyl radical, or one of R_3 and R_4 represents a lower alkyl radical, and the other represnts a hydrogen atom.

The compounds of formula I preferably contain a 1,2,4-triazol-1-yl group.

The present invention also relates to processes for the preparation of compounds of formula I. According to a feature of the invention such compounds are prepared by a process which comprises, when R_3 and R_4 both represent a hydrogen atom, the hydrogenation of a compound of formula IV, in which X, n, Ph, m, R_1 and R_2 are as hereinbefore defined, Hal represents a halogen atom, and Pr represents a protective group, such as 1-ethoxyethyl, or a hydrogen atom or, when one or each of R_3 and R_4 is other than a hydrogen atom, reaction of an organomagnesium compound of formula R_4MgX with a compound of formula IV and, if R_3 is other than hydrogen, addition of an alkyl halide of formula R_3X, cyclization of the compound of formula III thus obtained in which R_1, R_2, R_3, R_4, X, Hal, Ph, n and m are as hereinbefore defined, Z is a hydrogen atom or OZ is a leaving group, and the introduction of an imidazole or triazole ring into the compound of formula II in which R_1, R_2, R_3, R_4, X, Ph, m and n are as hereinbefore defined and Y represents an atom or a group which can be removed by a nucleophilic substitution to introduce the imidazole or triazole ring, the groups oPr and Hal being converted, if necessary, to groups OZ and Y respectively.

When R_3 and R_4 both represent a hydrogen atom, the compounds of formula III are preferably obtained by the hydrogenation of a compound of formula IV using an equimolecular quantity of hydrogen in the presence of a

suitable catalyst, which may be poisoned; the catalyst is preferably palladium, ruthenium, Raney nickel, platinum or rhodium deposited on an inert support and most preferably palladium, optionally poisoned (e.g. by pyridine or quinoline) which gives specifically the cis-olefin.

The hydrogenation may be carried out in a homogeneous or a heterogeneous phase.

Palladium in the metallic state, deposited on an inert support such as carbon black, calcium carbonate or barium sulphate is preferred.

Although it is not essential, the reaction is advantageously carried out in a protic polar solvent, e.g. in a lower alcohol such as methanol or in an aprotic solvent, e.g. toluene.

The concentration of the compound of formula IV is preferably from 1 to 80% by weight and more preferably from 5 to 40% relative to the total solution.

Although the molar proportion of the catalyst relative to the compound of formula IV may vary considerably, it is preferable to use the catalyst in a molar proportion of from 0.01 to 0.5% relative to the compound of formula IV.

The hydrogenation is generally carried out at temperatures of from -20°C to +150°C and preferably from 15 to 80°C and at a pressure of 1 to 10 atmospheres (which is 0.1 to 1 MPa).

The compound of formula IV may be obtained by methods known per se, e.g. by the reaction of an organometallic compound of formula:

$$R_2-(OPr)CH-C\equiv C-M$$

in which M is an alkali metal or a magnesium-containing group (MgHal) or a zinc-containing group (ZnHal), and R_2 and Pr are as hereinbefore defined for example, with an acetophenone of formula:

$$(X)_n\ Ph(CH_2)_m\ COCH_2Hal$$

in which the various symbols are as hereinbefore defined. When Pr represents a protective group, it is essential to remove the protecting group from the alcohol before conversion into the OZ group and cyclization.

The preparation of the compound of formula IV may be carried out, e.g. in tetrahydrofuran, in a known manner.

When at least one of R_3 or R_4 does not represent a hydrogen atom, the preparation of the compounds of formula III is generally carried out as follows: reaction of the organomagnesium compound of formula R_4MgX (preferably 2 to 10 mol per 1 mol of IV) with a compound of general formula IV, in the presence or absence of copper iodide (preferably at from -20° to +80°C with 0.01 to 5 mol % of copper iodide), followed, if R_3 is other than hydrogen by the addition of the alkyl halide R_3X (generally 1 to 10

mol per 1 mol of the compound to which R_4MgX has been attached), in a solvent such as tetrahydrofuran, preferably at from -20° to +80°C. When an alkyl halide is not used it will be understood that the addition of R_4MgX is followed by a hydrolysis. The reaction with R_4MgX is preferably carried out in the presence of copper iodide.

The compounds of formula III (in which Z = H) may also be prepared by a process which comprises reacting an organomagnesium compound of formula R_3MgHal with an acetylenic alcohol of formula $R_4-C \equiv C-CR_1R_2-OH$ or reacting an organomagnesium compound of formula R_4Mg Hal with an acetylenic alcohol of formula $R_3-C \equiv C-CR_1R_2-OH$ (wherein the various symbols are as hereinbefore defined) generally in a solvent chosen from ethers, preferably tetrahydrofuran, or hydrocarbons such as benzene or toluene, in the presence of a cuprous halide, optionally complexed with a dialkyl sulphide and in a catalytic quantity (from 0.1 to 20 mol % relative to the organomagnesium compound R_3MgHal). The organomagnesium compound itself is generally employed in a molar quantity which is twice that of the acetylenic alcohol employed, at temperatures of from -60° to +50°C, preferably from -30° to +20°C. An organomagnesium reagent of formula XIV is thus prepared as described in J.F. Normant and A. Alexakis, Synthesis (1981) 841-870.

The organomagnesium compound of formula XIV is condensed with a haloacetophenone of formula $(X)_nPh(CH_2)_mCOCH_2Hal$, in which the various symbols are as

hereinbefore defined under conditions similar to the procedures described above for the preparation of compounds of formula V.

A compound of formula III may also be converted into a compound of formula I by the following sequence of reactions:

a compound of formula III (in which Z = H) is acylated (by methods known per se, e.g. with an aliphatic or aromatic acyl halide or alternatively with an anhydride, in the presence of a base such as pyridine) to obtain a compound of formula III (in which Z = acyl), which is then condensed with a triazole or imidazole to obtain a compound of formula XIII; the group Z is then saponified to prepare the corresponding compound in which Z is hydrogen; the cyclization of a compound of formula XIII may then be carried out according to the procedures described below, and in specific cases (especially in the cases where $(X)_n$ represents substitution in the ortho position of the aromatic ring and if m = 0), the compounds of formula I are formed directly from the compounds of formula III (in which Z = acyl) under the conditions for condensing the triazole or imidazole and the compounds of formula XIII (in which Z = acyl) are not isolated in these cases.

The synthesis of the compounds of formula II, when Y represents a halogen atom, comprises cyclizing the compound of formula III (preferably in the cis-form) in which X, Ph, Hal, n, m, R_1, R_2, R_3 and R_4 are as hereinbefore defined either in an acid medium if Z is a

hydrogen atom, or in a basic medium if Z is a leaving group such as a mesylate, a tosylate, a triflate or a group of formula $[Ph_3P^+-O-]$.

The leaving groups are selectively attached to the hydroxy group by methods known per se, without affecting the tertiary hydroxyl group.

Organic or inorganic acid catalysts are suitable for the cyclization. The latter may be soluble or insoluble in the reaction medium, and protic or aprotic. Hydrochloric, sulphuric, trifluoroacetic, perchloric, benzenesulphonic, toluenesulphonic and methanesulphonic acids may be mentioned as protic acids. Lewis acids such as BF_3, $AlCl_3$ and $SnCl_4$ may be mentioned as aprotic acids.

0.1 to 2 molar equivalents of acid per mol of compound of formula III will preferably be employed.

The cyclization may also be carried out using catalysts bound to inert supports such as sulphonic resins.

The cyclization is usually carried out by simple heating of the reagents mentioned. The temperatue is generally from 10°C to 100°C or, if a solvent is present, from 10°C to the boiling point of the solvent.

Aliphatic and aromatic solvents such as toluene, ethers and ketones may be mentioned among the many solvents which can be used.

In the case of cyclization in a basic medium, inorganic bases, e.g. sodium hydroxide or potassium hydroxide, alkali metal or alkaline earth metal carbonates, nitrogeneous bases such as triethylamine, quaternary amines

such as tetrabutylammonium hydroxide or phosphonium hydroxides are suitable. 0.1 to 2 molar equivalents of the base per mol of compound of formula III are preferably employed. The cyclization may also be carried out using catalysts bound to inert supports such as resins. The reaction is usually carried out at a temperature of from 10°C to 100°C or if a solvent such as aliphatic and aromatic solvents, ethers and ketones is present, at from 10°C to the reflux temperature of the reaction mixture.

Compounds of formula II in which Y represents a hydroxy group may be obtained by treating the compounds of general formula III in which Z = H with a base.

This involves passing through the corresponding epoxides resulting from the products of general formula VI. It is generally essential, after isomerization, to convert the group Y = hydroxy into a leaving group (e.g. mesylate, tosylate, triflate or Ph_3P^+-O) before carrying out the substitution reaction with imidazole or triazole as described below.

The introduction of an imidazole or triazole into the compound of formula II is advantageously carried out in the presence of an acid acceptor in an anhydrous or a non-anhydrous medium, in a solvent which is inert under the reaction conditions, generally from 50 to 180°C and preferably at a temperature near to the boiling point of the solvent. Inorganic bases, e.g. sodium hydroxide or potassium hydroxide, alkali metal or alkaline earth metal carbonates, nitrogenous bases such as triethylamine,

quaternary amines such as tetrabutylammonium hydroxide, or phosphonium hydroxides may be mentioned as acid acceptors. Polar aprotic solvents e.g. dimethylformamide, dimethylacetamide, dimethyl sulphoxide, acetone, methyl ethyl ketone, methyl isobutyl ketone, acetonitrile, N-methylpyrrolidone or polar protic solvents such as methanol or propanol or butanol may advantageously be employed as solvents. If desired, the reaction may be carried out in the presence of a suitable catalyst. Phase-transfer catalysts e.g. quaternary ammonium derivatives such as tetrabutylammonium halides, and preferably iodides, may be mentioned as the catalyst which may be employed.

An alkali metal, phosphonium or ammonium derivative of an imidazole or triazole, optionally formed in situ, is preferably used. The reaction is preferably carried out with a molar excess, preferably of from 1.05 to 1.5, of the triazole or imidazole derivative.

The reaction is preferably carried out in a solvent containing from 1% to 70% by weight of compound of formula II relative to the total solution.

The acid acceptor is preferably present in a quantity not less than the stoichiometric quantity in equivalents of labile hydrogen atoms in the triazole or imidazole. A ratio in molar equivalents of from 1 to 2.5 is generally satisfactory.

It will be understood that a salt of the triazole or the imidazole may be prepared separately and the

presence of an acid acceptor is then not required for the reaction with the compound of formula II. This is carried out in an anhydrous or non-anhydrous medium in a solvent, under the same reaction conditions as those described for the formation in situ of a salt of the triazole or imidazole.

According to a further feature of the invention the compounds of formula I may be prepared by the process which comprises reaction of a haloacetophenone of formula: $(X)_nPh(CH_2)_mCOCH_2Hal$ with an organometallic compound of formula: $R_2R_1C{=}CR_3{-}CHR_4M$ in which X, m, n, Hal, Ph, and R_1 to R_4 are as hereinbefore defined and M represents an alkali metal, a magnesium-containing or a zinc-containing group eg. Mg Hal or Zn Hal to obtain a compound of formula V,

introducing a triazole or imidazole ring into the compound of formula V in which X, m, n, Hal and R_1 to R_4 are as hereinbefore defined to obtain a compound of formula VI,

addition of a halogen or mixed halogen molecule to the compound of formula VI to obtain a compound of formula VIII,

cyclization of the compound of formula VIII to obtain a compound of formula IX, and

reacting the compound of formula IX with a base to obtain the compound of formula I.

The reaction of the haloacetophenone of formula: $(X)_nPh(CH_2)_mCOCH_2Hal$ with an organometallic compound of

formula $R_2R_1C=CR_3-CHR_4M$ in which X, m, n, M, Hal, R_1, R_2, R_3 and R_4 are as hereinbefore defined is generally carried out in a solvent which is preferably an ether such as diethyl ether or tetrahydrofuran or an aliphatic, alicyclic or aromatic hydrocarbon such as hexane or toluene, at a temperature from -50°C to the reflux temperature of the solvent concerned and in a molar ratio ketone : organometallic compound preferably from 1.1 to 0.2: after neutralizing the reaction medium, the reaction leads to the compound of formula V.

The introduction of a triazole or imidazole ring into the compound of formula V may be carried out as hereinbefore described for the introduction of a triazole or imidazole ring into a compound of formula III.

The compound of formula V is generally reacted with an unsubstituted triazole or imidazole in the presence of an organic or inorganic base, e.g. pyridine, triethylamine, sodium hydroxide, potassium hydroxide or an alkali metal or alkaline earth metal carbonate or bicarbonate and in a suitable solvent, e.g. alcohols, ketones, amides, nitriles and optionally halogenated aromatic hydrocarbons, at a temperature from 80° to the reflux temperature of the solvent and in a molar ratio compound V : imidazole or triazole preferably from 1.1 to 0.2, which leads to the compound of formula VI. The reaction generally passes through an epoxide intermediate of formula VII which may be isolated, or prepared separately by methods known per se.

The addition of halogen or of mixed halogen to the compound of formula VI, preferably mol per mol, is generally carried out in an inert solvent such as saturated hydrocarbons or optionally halogenated aromatic hydrocarbons.

The compound of formula IX is preferably obtained at ambient temperature by cyclizing the compound of formula VIII in the presence of an organic or inorganic base mentioned above, in a molar ratio compound VIII : base preferably from 1.1 to 0.66. The reaction may be carried out in a protic or aprotic solvent medium (e.g. water, alcohol, ketone, nitrile, ester, saturated hydrocarbon or optionally halogenated aromatic hydrocarbon, dimethyl sulphoxide or amide such as dimethylformamide).

In a modification of the process of the invention the compounds of formula IX are prepared by introducing the imidazole or triazole ring after the cyclization, using the same procedure for the different stages. Thus, a molecule of halogen or of halogen halide (mixed halide) is reacted with a compound of formula V to give a compound of formula X, the latter then being cyclized to give a compound of formula XI, into which a triazole or imidazole group is introduced to give a compound of formula IX.

In order to obtain compound I, compound IX is reacted with a base. Suitable bases include inorganic bases e.g. sodium hydroxide or potassium hydroxide and alkali metal or alkaline earth metal carbonates, nitrogenous bases such as triethylamine, quaternary amines

such as tetrabutyl-ammonium hydroxide or phosphonium hydroxides.

1 to 5 molar equivalents of base is preferably employed per mol of compound of formula IX. The reaction is advantageously carried out in the presence of a solvent. Aprotic polar solvents e.g. dimethylformamide, dimethylacetamide, dimethyl sulphoxide, acetone, methyl ethyl ketone, methyl isobutyl ketone, acetonitrile and N-methylpyrrolidone or protic polar solvents such as methanol or propanol or butanol are advantageously employed as solvents. The temperature is generally from the ambient temperature to the reflux temperature of the solvent.

According to a further feature of the invention the triazole or the imidazole ring is introduced into a compound of formula IV or III to obtain a compound of formula XII or XIII, respectively, and then hydrogenating in the case of the compound of formula XII, and cyclizing preferably under the same conditions as those hereinbefore described.

The introduction of the imidazole and triazole ring is preferably carried out as hereinbefore described for the introduction of an imidazole or triazole ring into a compound of formula II.

The hydrogenation is preferably carried out as hereinbefore described for the hydrogenation of a compound of formula IV.

The cyclizing is preferably carried out as hereinbefore described for the cyclisation of a compound of

formula III.

According to a further feature of the invention the compound of formula XIII (in which Z = H) may also be obtained by reacting an azolylacetophenone, (which may be obtained by introducing a triazole or imidazole ring into a haloacetophenone of formula $(X)_n Ph(CH_2)_m COCH_2 Hal$ under the conditions hereinbefore described) with an organomagnesium compound of formula XIV.

According to a further feature of the invention a compound of formula X is reacted with an imidazole or a triazole in the presence of an excess (2 mol or more) of a base to obtain a compound of formula IX directly.

According to a further feature of the invention a compound of formula VII is halogenated and an imidazole or triazole group is then introduced to obtain a compound of formula VIII.

The compound of formula I formed is isolated from the reaction medium by any method known per se e.g. by distilling off the solvent, or by crystallizing the compound from the reaction medium, or by filtration and, if necessary, the compound is then purified by known methods such as recrystallization in a suitable solvent.

The present invention relates to the compounds of formula II to XIII, in which X, m, n, Ph, R_1 to R_4, Hal, W, Z, Pr and Y are as hereinbefore defined.

The invention also provides a method for the control of fungal diseases of crops at a locus which comprises applying thereto a compound of formula I or an

agriculturally acceptable salt or complex thereof with a metal salt.

The compounds of formula I may be used for the preventive as well as the curative control of fungi, especially of the basidiomycetes, ascomycetes, adelomycetes or fungi imperfecti type, in particular rusts, mildew, eyespot, fusarium diseases, helminthosporium diseases, septoria diseases and rhizoctonia diseases of crops and of plants in general and, in particular, of cereals such as wheat, barley, rye, oats and their hybrids and also rice and maize. The compounds of formula I are active, in particular, against fungi, especially of the basidiomycetes, ascomycetes, adelomycetes or fungi imperfecti type such as Botrytis cinerea, Erysiphe graminis, Puccinia recondita, Piricularia oryzae, Cercospora beticola, Puccinia striiformis, Erysiphe cichoracearum, Fusarium oxysporum (melonis), Pyrenophora avenae, Septoria tritici, Venturia inaequalis, Monilia laxa, Mycosphaerella fijiensis, Marssonina panettoniana, Alternaria solani, Aspergillus niger, Cercospora arachidicola, Cladosporium herbarum, Helminthosporium oryzae, Penicillium expansum, Pestalozzia sp, Phialophora cinerescens, Phoma betae, Phoma foveata, Phoma lingam, Ustilago maydis, Verticillium dahliae, Ascochyta pisi, Guignardia bidwellii, Corticium rolfsii, Phomopsis viticola, Sclerotinia sclerotiorum, Sclerotinia minor, Coryneum cardinale and Rhizoctonia solani.

They are also active against

the following fungi: Acrostalagmus koningi, the Alternaria, the Colletotrichum, Corticium rolfsii, Diplodia natalensis, Gaeumannomyces graminis, Gibberella fujikuroi, Hormodendron cladosporioides, Lentinus degener or tigrinus, Lenzites quercina, Memnoniella echinata, Myrothecium verrucaria, Paecylomyces varioti, Pellicularia sasakii, Phellinus megaloporus, Polystictus sanguineus, Poria vaporaria, Sclerotium rolfsii, Stachybotris atra, the Stereum, Stilbum sp, Trametes trabea, Trichoderma pseudokoningi and Trichothecium roseum.

The compounds of the invention are of special interest because of their broad spectrum as regards cereal diseases (mildew, rust, eyespot, net blotch, leaf spot and foot root). They are also of great interest because of their effectiveness against grey mould (Botrytis) and Cercospora diseases and, because of this, they may be applied to crops as varied as grape vine, vegetable crops and tree crops and tropical crops such as peanut, banana, coffee, pecan nut and others.

In addition to the applications already described above, the compounds according to the invention additionally have an excellent biocidal activity with respect to many other species of microorganisms, among which there may be mentioned, fungi such as those which belong to the genera:
Pullularia, such as the species P. pullulans, Chaetomium, such as the species C. globosum, Aspergillus, such as the species Aspergillus niger, and Coniophora, such as the

species C. puteana.

Owing to their biocidal activity, the compounds of the invention make it possible to control effectively microorganisms the proliferation of which gives rise to many problems in the agricultural and industrial fields. To this end, they are particularly well suited to the protection of plants or of industrial products such as wood, leather, paints, paper, ropes, plastics and industrial water systems.

They are most particularly well suited to the protection of lignocellulose products and especially of wood, whether it is timber for furniture or construction, or timber which is exposed to adverse weather conditions such as timber for fencing, vine stakes or railway sleepers.

The compounds according to the invention, used on their own or in the form of compositions as defined hereinafter in the treatments of wood, are generally employed with organic solvents and may be used, if required, in combination with one or more known biocidal products such as pentachlorophenol, metal salts, especially copper, manganese, cobalt, chromium or zinc salts derived from inorganic or carboxylic acids (heptanoic, octanoic or naphthenic acids); organic complexes of tin, mercaptobenzothiazole, insecticides such as pyrethroids or organochlorine compounds.

Finally, they have an excellent selectivity with respect to crops.

They are advantageously applied at doses of 0.005 to 5 kg/ha, and more specifically 0.01 to 0.5 kg/ha.

In practical use, the compounds according to the invention are rarely used alone. Most often they form part of compositions. The present invention provides compositions, which can be used for the protection of plants against fungal diseases, or in plant growth-regulating compositions, which compositions comprise, as active ingredient, a compound of formula I or an agriculturally acceptable salt or complex with a metal salt in association with an agriculturally acceptable carrier. The carrier may be solid or liquid. The composition may also comprise an agriculturally acceptable surfactant. Conventional inert carriers and conventional surfactants can especially be used.

The term "carrier", in the present description, denotes a natural or synthetic organic or inorganic substance, with which the active substance is combined in order to facilitate its application to the plant, to seeds or to the soil. Therefore, this carrier is generally

inert and it must be acceptable in agriculture, especially on the treated plant. The carrier may be solid (clays, natural or synthetic silicates, silica, resins, waxes, solid fertilizers etc) or liquid (water, alcohols, ketones, petroleum fractions, aromatic or paraffinic hydrocarbons, chlorinated hydrocarbons, liquified gases etc).

The surfactant may be an emulsifier, dispersant or wetting agent of the ionic or the nonionic type. For example, there may be mentioned polyacrylic acid salts, lignosulphonic acid salts, phenolsulphonic or naphthalenesulphonic acid salts, polycondensates of ethylene oxide with fatty alcohols or with fatty acids or with fatty amines, substituted phenols (especially alkyl phenols or aryl phenols), sulphosuccinic acid ester salts, taurine derivatives (especially alkyl taurates), phosphoric acid esters of alcohols or of polycondensates of ethylene oxide with phenols. The presence of at least one surfactant is generally indispensable when the active substance and/or the inert carrier are insoluble in water and the vector agent for the application is water.

Therefore, for their application, the compounds of formula (I) are generally in the form of compositions; these compositions according to the invention are themselves in fairly diverse solid or liquid forms.

As solid forms of compositions, there may be mentioned powders for dusting or scattering (with a content

of the compound of formula (I) which may range up to 100%) and granules, especially those obtained by extrusion, by compacting, by impregnating a granulated carrier, or by granulation starting with a powder (the content of the compound of formula (I) in these granules being between 1 and 80% in these latter cases).

As liquid forms of compositions, or forms intended to constitute liquid compositions when applied, there may be mentioned solutions, especially water-soluble concentrates, emulsifiable concentrates, emulsions, flowables, aerosols, wettable powders (or powder for spraying) and pastes.

The emulsifiable or soluble concentrates generally contain 10 to 80% of active substance, whereas the emulsions or solutions ready for application contain, for their part, 0.01 to 20% of active substance.

These compositions may also contain any other type of ingredients such as, e.g. protective colloids, adhesives, thickeners, thixotropic agents, penetrants, stabilizers, sequestering agents, as well as other known active substances with pesticidal properties (especially insecticidal or fungicidal properties) or with properties which promote plant growth (especially fertilizers) or with plant growth-regulating properties. More generally, the compounds according to the invention may be combined with all the solid or liquid additives which correspond to the usual techniques of formulation.

For example, in addition to the solvent, the emulsifiable concentrates may contain, when required, 2 to 20% of suitable additives such as the stabilizers, surfactants, penetrants, corrosion inhibitors, colouring agents or adhesives mentioned above.

In the case where the compounds according to the invention are used as fungicides, the doses for use may vary within wide limits according, in particular, to the virulence of the fungi and the climatic conditions.

In general, compositions containing 0.5 to 5,000 ppm of active substance are very suitable; these values apply to the compositions ready for application. Ppm means "parts per million". The range from 0.5 to 5,000 ppm corresponds to a range from 5×10^{-5} to 0.5% (percentages by weight).

As regards compositions which are suitable for storage and transportation, they more advantageously contain from 0.5 to 95% (by weight) of active substance.

Thus, the compositions for agricultural use according to the invention may contain active substances according to the invention within very wide limits, ranging from 5×10^{-5}% to 95% (by weight).

By way of example, the compositions of some concentrates are given below:

Example F (formulation) 1

Active substance	400 g/l
Alkali metal dodecylbenzenesulphonate	24 g/l

10:1 ethylene oxide/nonylphenol condensate	16 g/l
Cyclohexanone	200 g/l
Aromatic solvent q.s.	1 litre

According to another formula for an emulsifiable concentrate, the following are used:

Example F 2:

Active substance	250 g
Epoxidized vegetable oil	25 g
Mixture of alkylarylsulphonate, polyglycol ether and fatty alcohols	100 g
Dimethylformamide	50 g
Xylene	575 g

From these concentrates it is possible to obtain, by dilution with water, emulsions of any desired concentration, which are especially suitable for application to leaves.

Flowables, which can also be applied by spraying, are prepared so as to obtain a stable fluid product which does not settle and they usually contain from 10 to 75% of active substance, from 0.5 to 15% of surfactants, from 0.1 to 10% of thixotropic agents and from 0 to 10% of suitable additives such as antifoams, corrosion inhibitors, stabilizers, penetrants and adhesives, and, as a carrier, water or an inorganic liquid in which the active substance is of low solubility or insoluble: some solid organic substances or inorganic salts may be dissolved in the carrier to assist in preventing sedimentation, or as

antifreezes for water.

The wettable powders (or powders for spraying) are usually prepared so as to contain 20 to 75% of active substance, and they usually contain, in addition to the solid carrier, from 0 to 5% of a wetting agent, from 3 to 10% of a dispersant, and, when required, from 0 to 10% of one or more stabilizers and/or other additives such as penetrants, adhesives, or anticaking agents, colouring agents.

By way of example, various compositions of wettable powders are given below:

Example F 3:

Active substance	50%
Calcium lignosulphonate (deflocculant)	5%
Isopropyl naphthalene sulphonate (anionic wetting agent)	1%
Anticaking silica	5%
Kaolin (filler)	39%

Another composition of powder for spraying, at a concentration of 70%, uses the following constituents:

Example F 4:

Active substance	700 g
Sodium dibutylnaphthalenesulphonate	50 g
Condensation product of naphthalenesulphonic acid, phenolsulphonic acid and formaldehyde in proportions 3:2:1	30 g
Kaolin	100 g

Chalk	120 g

Another composition of powder for spraying, at a concentration of 40%, uses the following constituents:

Example F 5:

Active substance	400 g
Sodium lignosulphonate	50 g
Sodium dibutylnaphthalenesulphonate	10 g
Silica	540 g

Another composition of powder for spraying, at a concentration of 25%, uses the following constituents:

Example F 6:

Active substance	250 g
Calcium lignosulphonate	45 g
Mixture of chalk and hydroxyethylcellulose in equal parts by weight	19 g
Sodium dibutylnaphthalenesulphonate	15 g
Silica	195 g
Chalk	195 g
Kaolin	281 g

Another composition of powder for spraying, at a concentration of 25%, uses the following constituents:

Example F 7:

Active substance	250 g
Isooctylphenoxy-polyoxyethylene-ethanol	25 g
Mixture of chalk and hydroxyethylcellulose in equal parts by weight	17 g
Sodium aluminosilicate	543 g

Kieselguhr	165 g

Another composition of powder for spraying, at a concentration of 10%, uses the following constituents:

Example F 8:

Active substance	100 g
Mixture of sodium salts of sulphates of saturated fatty acids	30 g
Condensation product of naphthalenesulphonic acid and formaldehyde	50 g
Kaolin	820 g

In order to obtain these powders for spraying or wettable powders, the active substances are intimately mixed in suitable mixers with additional substances, and the mixtures are ground in mills or other suitable grinders. Powders for spraying are thereby obtained, the wettability and the suspendability of which are advantageous; they may be suspended in water at any desired concentration and these suspensions may very advantageously be used, especially for application to plant leaves.

Instead of the wettable powders, pastes can be produced. The conditions and steps of production and use of these pastes are similar to those for wettable powders or powders for spraying.

As already stated, the dispersions and aqueous emulsions, e.g. the compositions obtained by diluting with water a wettable powder or an emulsifiable concentrate according to the invention, are included within the

general scope of the present invention. The emulsions may be of the water-in-oil or oil-in-water type, and they may have a thick consistency like that of a "mayonnaise".

Granules intended for placing on the soil are usually prepared so as to be between 0.1 and 2 mm in size and they may be manufactured by agglomeration or impregnation. In general, the granules contain 0.5 to 25% of active substance and 0 to 10% of additives such as stabilizers, slow-release modification agents, binders and solvents.

According to an example of granule composition, the following constituents are used:

Example F 9:

Active substance	50	g
Epichlorhydrin	2.5	g
Cetyl polyglycol ether	2.5	g
Polyethylene glycol	35	g
Kaolin (particle size: 0.3 to 0.8 mm)	910	g

In this particular case, the active substance is mixed with epichlorhydrin and dissolved in 60 g of acetone; polyethylene glycol and cetyl polyglycol ether are then added. The kaolin is wetted with the solution obtained and the acetone is then evaporated off under vacuum. A microgranule of this type is advantageously used to control soil fungi or pathogenic fungi of stems and aerial parts treated by application to the soil or in water, particularly in rice fields.

The compounds of formula (I) may also be used in

the form of powders for dusting; a composition containing 50 g of active substance and 950 g of talcum may also be used; a composition containing 20 g of active substance, 10 g of finely divided silica and 970 g of talcum may also be used; these constituents are mixed and ground, and the mixture is applied by dusting.

The following examples illustrate the invention:

Example 1: Preparation of 2-(2,4-dichlorophenyl)-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

A solution of 2-chloromethyl-2-(2,4-dichlorophenyl)-2,5-dihydrofuran (1.001 g; 3.80 mmol) in N-methylpyrrolidone (N.M.P.) (1.00 g) is introduced into a 50-ml round-bottomed flask, under an inert atmosphere. 1,2,4-Triazole (314.8 mg; 4.56 mmol) and potassium carbonate (630.2 mg; 4.56 mmol) are then added. The reaction medium is heated at a temperature of 170°C for 14 hours and is then cooled to approximately 20°C. Toluene (10 cc) and then water saturated with ammonium chloride are then added. The toluene phase is collected, the aqueous phase is further extracted with toluene (2 x 10 cc). The combined organic extracts are dried over sodium sulphate. After filtering and concentrating under reduced pressure, a semi-crystalline residue is obtained, which is purified.

Weight obtained: 673 mg (2.28 mmol); m.p. (Kofler): 107°C.

Yield: 60% relative to the starting 2,5-dihydrofuran.

Preparation of 2-chloromethyl-2-(2,4-dichlorophenyl)-2,5-dihydrofuran

1-Chloro-2-(2,4-dichlorophenyl)-3-pentene-2,5-diol (cis-isomer) (10 g; 35.5 mmol) in 60 ml of toluene is introduced into a 100-ml round-bottomed flask under an inert atmosphere. Para-toluenesulphonic acid (0.5 g) is added and the mixture is heated under reflux. When the reaction is complete, washing and separation are carried out. A brown oil residue (9.36 g; 35.5 mmol) is obtained. Yield: 100% relative to the starting product.

Preparation of 1-chloro-2-(2,4-dichlorophenyl)-3-pentene-2,5-diol (cis-isomer)

Method A:

1-Chloro-2-(2,4-dichlorophenyl)-5-(1-ethoxyethoxy)-3-pentyn-2-ol (24 g) dissolved in toluene (150 cc) and palladinized charcoal (0.613 g) containing 5% palladium are introduced into a 500-ml round-bottomed flask under an inert atmosphere. The flask is supplied with hydrogen at atmospheric pressure, at 25°C. After 2 hours, filtration is carried out and the solvent is removed under reduced pressure.

The oily residue is taken up with methanol (200 cc) and 0.5 N hydrochloric acid (50 ml) is added. The methanol is then removed under reduced pressure and an orange oily residue (19.36 g) is obtained.

The addition of ethyl acetate (10 cc) and then pentane (35 cc) enables the desired diol (5.35 g; 19.3 mmol) to be precipitated.

Preparation of 1-chloro-2-(2,4-dichlorophenyl)-5-(1-ethoxyethoxy)-3-pentyn-2-ol

Bromoethane (54.5 g; 0.5 mol) dissolved in tetrahydrofuran (225 cc) is poured into a 500-ml round-bottomed flask containing magnesium (13.37 g) and THF (30 cc), under an inert atmosphere, at T = 30°C. The solution obtained is poured dropwise onto a solution of 2-ethoxyethyl propargylether (64.09 g; 0.5 mol) in THF (40 cc), in the course of 1 hour at ambient temperature. A solution of 2,4,2'-trichloroacetophenone (89.4 g; 0.4 mole) in THF (100 cc) is poured into the above solution at 0°C in the course of 2 hours. The mixture is maintained for 6 h at 20°C. It is cooled to 0°C and acetic acid (28.6 cc; 0.5 mol) is added at 5°C in the course of 15 minutes, followed by the addition of water (150 cc) and then ethyl ether (100 cc). The organic phase is washed with water (2 x 50 cc) and once with brine (50 cc) and the solvents are then removed under reduced pressure. A viscous yellow oil (136.6 g) is obtained.

Yield: 97.2% relative to the starting product.

Method B:

Bromoethane (163.45 g) in toluene (250 cc) is poured into a 1-l round-bottomed flask containing magnesium (36.5 g; 1.5 mol) and THF (216 g) and dissolved toluene (75 cc) under an inert atmosphere, at 30°C, in the course of 1 h 15 min. The mixture is allowed to stand for 15 min at 24°C. A propargyl alcohol solution (42.15 g;

0.75 mol) in toluene (50 cc) is poured in dropwise in the course of 1 h 30 min. A solution of 2,4,2'-trichloroacetophenone (111.7 g; 0.5 mol) in toluene (100 cc) is added dropwise at 44°C. The mixture is allowed to stand at ambient temperature. The medium is then cooled to 0°C and acetic acid (90 g; 1.5 mol) is added dropwise. Evaporation is carried out, toluene (250 cc) is added and washing is carried out with dilute sulphuric acid and then with water. The organic phase is then concentrated, cooled, precipitated, filtered and dried. 1-Chloro-2-(2,4-dichlorophenyl)-3-pentyne-2,5-diol is obtained. M.p. = 90°C. Hydrogenation is carried out in the same manner as in Method A, but at 50°C. The desired diol is obtained.

Preparation of the compound of Example 1 according to another method.

Stage .) Preparation of 1-chloro-2-(2,4-dichlorophenyl)-4-penten-2-ol

An organomagnesium derivative is prepared by adding a solution of allylbromide (110 cc) in ethyl ether (700 cc) to tetrahydrofuran (200 cc) containing magnesium (110 g), between 15 and 20°C, in the course of three hours. The mixture is heated under reflux for 30 min, decanted, the organic phase is evaporated off and the residue is washed with ether.

A solution of alpha,2,4-trichloroacetophenone (175 g) in tetrahydrofuran (250 g) is added at -30°C and the solution is neutralized with acetic acid. Washing

with water, drying over sodium sulphate, concentration and then distillation under vacuum are carried out. A colourless oil is obtained (205 g). M.p. (3×10^{-2} mm Hg) = 140-142°C.

Stage b) Preparation of 1-[2-(2,4-dichlorophenyl)-2-hydroxy-4-pentenyl]-1H-1,2,4-triazole

A mixture of product obtained in stage a) (106 g), triazole (55 g) and potassium carbonate (160 g) is heated for four hours at 120°C in dimethylformamide (600 cc). The insolubles are filtered, washed with dimethylformamide and the reaction mixture is concentrated under vacuum. The residue, dissolved in methylene chloride, is washed with water and then concentrated. The product is obtained by crystallization in ethyl acetate after dilution with heptane. A light pink solid (97 g) is isolated. M.p. = 101°C.

Stage c) Preparation of 1-[4-bromo-2-(2,4-dichlorophenyl)-tetrahydrofuran-2-ylmethyl]-1H-1,2,4-triazole

The compound obtained in stage b) (35 g) in chloroform (200 cc) is treated at 0°C with bromine. After decolourizing, the solvent is evaporated off and the residue is redissolved in methanol. An aqueous potassium hydroxide solution is then added until a basic pH is obtained. After evaporating the medium under vacuum, the residue is extracted with ethyl acetate, washed with water and concentrated. The oil obtained (40 g) consists of a mixture of two diastereoisomers in substantially equal proportions.

By chromatography on silica, the following isomers are isolated in sequence: least polar isomer No. 1a: white crystals, m.p. 83°C, followed by the most polar isomer No. 1b: white crystals, m.p. 94°C. After recrystallization, isomers 1a, m.p. 96°C and 1b, m.p. 104°C, are obtained.

Stage d) Preparation of 2-(2,4-dichlorophenyl)-2-[(1-triazolyl)methyl]-2,5-dihydrofuran

The isomer a (30 g; 795 mmol), methanol (200 cc) and 85% potassium hydroxide pellets (10.4 g; 159 mmol) are introduced into a 250-ml round-bottomed flask. The reaction medium is heated under reflux for 1 hour, cooled, filtered and concentrated. The residue is redissolved in chloroform (200 cc), filtered and evaporated. The semi-solid residue is recrystallized in ethyl acetate with 20% heptane.

Weight obtained: 19.4 g; m.p. = 107°C.

Example No. 2: Preparation of 2-(2,4-dichlorophenyl)-2-[(1,2,4-triazol-1-yl)methyl]-4-n-propyl-2,5-dihydrofuran (Compound No. 2)

A mixture of propargyl alcohol (7.8 cc; 0.132 mol), cuprous iodide (2.6 g; 0.014 mol) and dry tetrahydrofuran is placed in a 1-l round-bottomed flask under nitrogen and cooled to -10°C. An organomagnesium compound prepared starting with propyl bromide (34.4 g; 0.28 mol) and magnesium (7.2 g; 0.30 mol) in tetrahydrofuran (120 cc) is added dropwise at this temperature. After 15 hours at

ambient temperature, a solution of 2,4,2'-trichloroacetophenone (23.6 g; 0.106 mol) in tetrahydrofuran (140 cc) is added dropwise. After 2 hours, the medium is neutralized with glacial acetic acid, poured into water and extracted with ether, dried and then evaporated. An orange-coloured oil (17 g) consisting essentially of 2-(2,4-dichlorophenyl)-1-chloro-4-propyl-3-cis-pentene-2,5-diol is obtained, which is acetylated in the presence of acetic anhydride (5.6 cc) in pyridine (30 cc). After leaving overnight at ambient temperature, the pyridine is co-evaporated with the toluene and the residue is heated at 130°C for 3 hours in the presence of potassium carbonate (25 g) and triazole (7 g) in dimethylformamide (250 cc). The medium is filtered, concentrated, diluted with water and extracted with dichloromethane. After evaporating off the solvent, the residue is chromatographed on silica (eluent: ethyl acetate:heptane 1:1) and this gives the compound 2 in the form of slightly yellow-coloured crystals (4.2 g), m.p. 85°C.

Example 3: Preparation of 2-(4-chlorophenyl)-2-[(1,2,4-triazol-1-yl)methyl]-4-ethyl-2,5-dihydrofuran

(Compound No. 3)

The reaction is carried out in the same way as in the above example, using ethyl bromide (27.2 g; 0.25 mol) and 4,2'-dichloroacetophenone (20.8 g; 0.11 mol). After condensing with triazole, the cyclization is not carried out and crude 2-(4-chlorophenyl)-1-(1,2,4-triazol-

1-yl)-4-ethyl-3-cis-pentene-2,5-diol monoacetate (20 g of a black oil) is essentially obtained. The latter is then saponified with potassium hydroxide (5.8 g) in methanol (250 cc) under reflux. After evaporation, dilution with water, extraction with dichloromethane and evaporation under vacuum, a black oil (17.5 g) is obtained. The latter, dissolved in dry dichloromethane (200 cc), is treated with methanesulphonyl chloride (4.9 cc) and then, at -30°C, with triethylamine added dropwise. After 2 hours, the medium is washed with water and concentrated and the residue, redissolved in methanol (200 cc), is treated with potassium hydroxide (3.8 g). After extracting with ethyl acetate and washing with water, the crude residue is chromatographed (eluent: ethyl acetate:heptane 1:1). The expected product is identified easily by its intense colour development with iodine in thin layer chromatography. The product 3 is obtained in the form of a partially crystallized brown oil.

Examples 4-15

Compounds Nos 4-15 of formula XV were prepared according to the methods described above.

Compounds of formula XV

-	X_1	Y_1	R_3	R_4	m.p.
1	Cl	Cl	H	H	107°
2	Cl	Cl	n-propyl	H	85°
3	Cl	H	ethyl	H	oil
4	Cl	H	H	H	124°
5	Cl	Cl	ethyl	H	86.5°
6	Cl	H	n-propyl	H	
7	Cl	Cl	4-fluorophenyl	H	
8	Cl	Cl	phenyl	H	
9	Cl	Cl	allyl	H	
10	Cl	H	allyl	H	
11	Cl	Cl	3-fluoropropyl	H	
12	Cl	H	3-fluoropropyl	H	
13	Cl	Cl	cyclopentyl	H	
14	Cl	H	cyclopentyl	H	
15	Cl	Cl	allyl	CH_3	

The chemical names of compounds 1 to 15 follow.

1 2-(2,4-Dichlorophenyl)-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

2 2-(2,4-Dichlorophenyl)-4-n-propyl-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

3 2-(4-Chlorophenyl)-4-ethyl-2-[1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

4 2-(4-Chlorophenyl)-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

5 2-(2,4-Dichlorophenyl)-4-ethyl-2-[(1,2,4-triazol-1-yl)-methyl]-2,5-dihydrofuran

6 2-(4-Chlorophenyl)-4-n-propyl-2-[(1,2,4-triazol-1-yl)-methyl]-2,5-dihydrofuran

7 2-(2,4-Dichlorophenyl)-4-(4-fluorophenyl)-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

8 2-(2,4-Dichlorophenyl)-4-phenyl-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

9 2-(2,4-Dichlorophenyl)-4-allyl-2-[(1,2,4-triazol-1-yl)-methyl]-2,5-dihydrofuran

10 2-(4-Chlorophenyl)-4-allyl-2-[(1,2,4-triazol-1-yl)-methyl]-2,5-dihydrofuran

11 2-(2,4-Dichlorophenyl)-4-(3-fluoro-n-propyl)-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

12 2-(4-Chlorophenyl)-4-(3-fluoro-n-propyl)-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

13 2-(2,4-Dichlorophenyl)-4-cyclopentyl-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

14 2-(4-Chlorophenyl)-4-cyclopentyl-2-[(1,2,4-triazol-

1-yl)methyl]-2,5-dihydrofuran

2-(2,4-Dichlorophenyl)-4-allyl-3-methyl-2-[(1,2,4-triazol-1-yl)methyl]-2,5-dihydrofuran

Example 16 - In vivo test on Erysiphe graminis in barley (barley mildew)

Barley, in pots, sown in plain soil, is treated at the 10-cm height stage by spraying with an aqueous emulsion (called slurry) of the active substance to be tested, having the following composition:

compound of Example 1 or 2: 60 mg

Tween 80 (surfactant) consisting of an oleate of a polycondensate derivative of ethylene oxide with sorbitan), diluted to 10% in water: 0.3 cc

made up to 60 cc with water.

This aqueous emulsion is then diluted with water to obtain the desired concentration. The trial is replicated twice. After 24 hours, the barley plants are dusted with Erysiphe graminis spores, the dusting being carried out using diseased plants.

Readings are taken 8 to 14 days after inoculation.

Under these conditions, a total protection is observed with the compounds 1, 2, 3, 4 and 5 at a dose of 1 g/l.

Example 17 - In vivo test on "Puccinia recondita" responsible for wheat rust

Wheat, in pots, sown in plain soil, is treated at the 10-cm height stage by spraying with aqueous emulsions (called slurries) of the same composition as that

described in Example 16.

After 24 hours, an aqueous suspension of spores (50,000 sp/cc) is sprayed onto the wheat; this suspension was obtained from contaminated plants. The wheat is then placed for 48 hours in an incubation cell at approximately 18°C and at 100% relative humidity.

After these 2 days, the relative humidity is lowered to 60%. The condition of the plants is verified between the 11th and the 15th days after inoculation, by comparison with the untreated control.

Total protection with the compounds 1, 2 and 5 at a dose of 1 g/l.

Example 18 - In vivo test on "Piricularia oryzae" responsible for rice blast

Rice, in pots, sown in a 50:50 mixture of peat and pozzolana, is treated at the 10-cm height stage by spraying with an aqueous emulsion (called slurry) defined above at the concentration indicated below. The trial is replicated twice. After 48 hours, treatment is carried out by applying to the leaves a suspension of spores obtained in pure culture.

Readings are taken 8 days after inoculation. Under these conditions, a total protection is observed with the compounds 1, 2, 3 and 5 at a dose of 1 g/l.

Example 19 - In vitro test on Botrytis cinerea in tomato

An aqueous suspension of the active substance to be tested, having the following composition, is prepared by

fine grinding:

active substance to be tested	60	mg
Tween 80 (surfactant consisting of a monolaurate of a polycondensate derivative of ethylene oxide with sorbitan)	0.6	cc
water	60	cc

This aqueous suspension is then diluted with water to obtain the desired concentration.

60- to 75-day-old, glasshouse-cultivated tomato plants (variety Marmande) are treated by spraying with aqueous suspensions of the composition described, at an active substance concentration of 1 g/l (1000 ppm). The trial is replicated twice with each concentration.

After 24 hours, the leaves are cut and placed in 2 Petri dishes (11 cm diameter), the bases of which have previously been provided with a moist filter paper disc (5 leaflets per dish).

The inoculum is then applied with a syringe by depositing drops (3 drops per leaflet) of a spore suspension. This suspension of Botrytis cinerea spores was obtained from a 15-day-old culture, which was then suspended in a nutrient solution (80,000 units/cc). Verification is carried out 4 to 6 days after inoculation by comparing with an untreated control. The percentage protection in comparison with the untreated control is thus determined.

Under these conditions, a total protection is

observed with the compounds 2 and 5, at a concentration of 0.33 g/l.

Example 20 - In vitro test on seed fungi and soil fungi

The action of the compounds according to the invention is studied on the following fungi responsible for diseases of cereals and other plants:

11) Pyrenophorae avenae
6) Septoria nodurum
12) Helminthosporium teres
9) Fusarium roseum
8) Fusarium nivale
7) Fusarium culmorum
13) Rhizoctonia cerealis
14) Septoria tritici
1) Botrytis cinerea sensitive to carbendazim and to cyclic imides
2) Botrytis cinerea resistant to carbendazim and to cyclic imides
5) Pseudocercosporella herpotrichoides
3) Fusarium oxysporum F.sp melonis
4) Rhizoctonia solani
10) Helminthosporium gramineum

The numbers which appear before the names will be used to identify the fungi in the table below.

For each trial, the procedure is as follows: a nutrient medium consisting of potato, glucose and agar PDA medium) is introduced supercooled into a series of

Petri dishes (20 cc per dish) after sterilizing in an autoclave at 120°C.

In the course of filling the dishes, a solution of the active substance in acetone is injected into the supercooled medium so as to obtain the desired final concentration.

Petri dishes similar to the above, into which are poured similar quantities of a nutrient medium which does not contain the active substance, are taken as control.

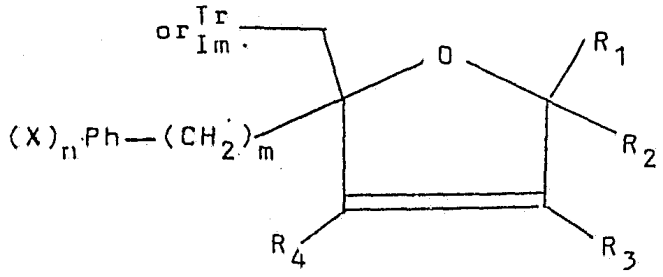
After 24 or 48 h, each dish is seeded by depositing a fragment of mycelium originating from a previous culture of the same fungus.

The dishes are stored for 2 to 10 days (depending on the fungus tested) at 22°C, and the growth of the fungus in the dishes containing the active substance to be tested is compared with that of the same fungus in the dish used as the control.

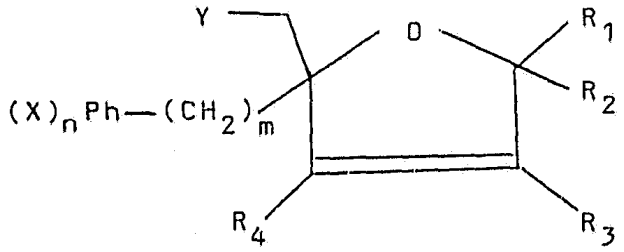
For each compound tested, the degree of inhibition of the fungus considered, at a dose of 30 ppm, is thus determined.

11	6	12	9	8	7	13	14	1	2	5	3	4	10
95	95	100	90	90	100	95	100	100	100	100	80	80	100
95	90	100	80	100	100	95	-	95	95	90	80	90	95
90	95	90	50	50	90	90	-	80	90	100	50	50	90
100	90	100	90	90	100	100	-	100	100	100	100	80	100
90	100	90	50	90	95	80	-	90	100	100	80	80	90

FORMULAE FOR THE COMPOUNDS



(I)

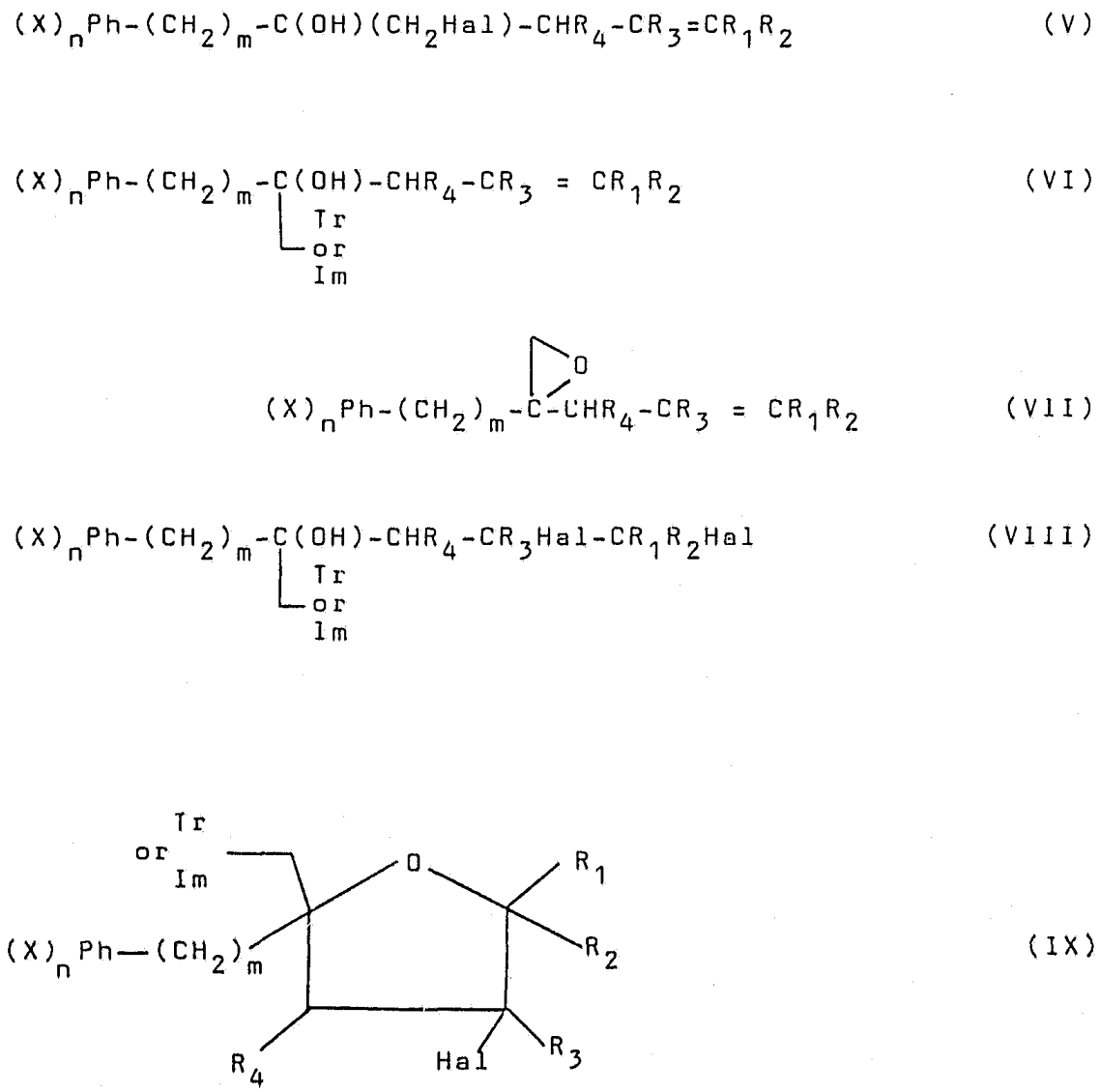


(II)

$(X)_nPh-(CH_2)_m-C(OH)(CH_2Hal)-CR_4=CR_3-CR_1R_2-OZ$ (III)

$(X)_nPh-(CH_2)_m-C(OH)\ (CH_2Hal)-C \equiv C-CR_1R_2OPr$ (IV)

FORMULAE FOR THE COMPOUNDS



$$(X)_nPh-(CH_2)_m-C(OH)(CH_2Hal)-CHR_4-CR_3=CR_1R_2 \qquad (V)$$

$$(X)_nPh-(CH_2)_m-C(OH)(Tr \text{ or } Im)-CHR_4-CR_3=CR_1R_2 \qquad (VI)$$

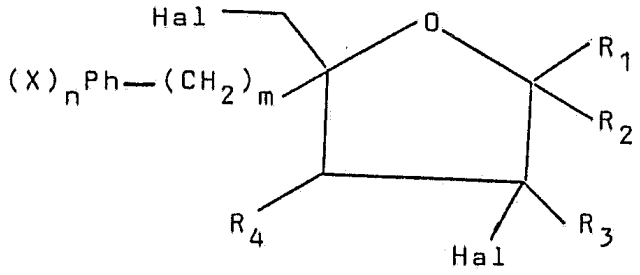
$$(X)_nPh-(CH_2)_m-C(\text{epoxide O})-CHR_4-CR_3=CR_1R_2 \qquad (VII)$$

$$(X)_nPh-(CH_2)_m-C(OH)(Tr \text{ or } Im)-CHR_4-CR_3Hal-CR_1R_2Hal \qquad (VIII)$$

(IX)

FORMULAE FOR THE COMPOUNDS

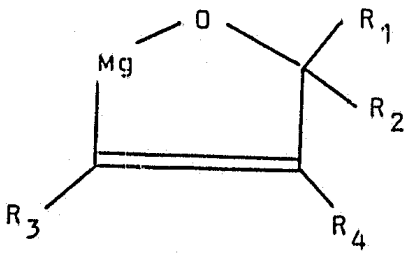
$$(X)_nPh\text{-}(CH_2)_m\text{-}C(OH)(CH_2Hal)\text{-}CHR_4\text{-}CR_3Hal\text{-}CR_1R_2Hal \qquad (X)$$



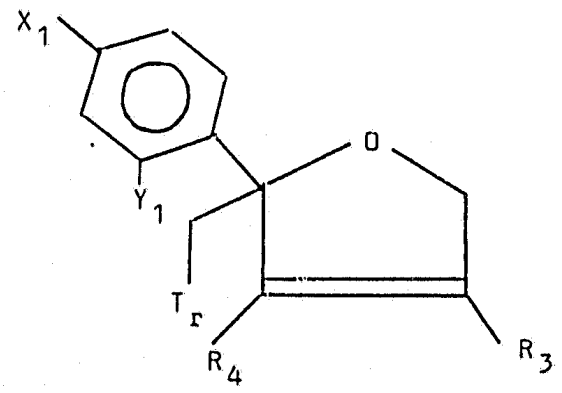
(XI)

$$(X)_nPh\text{-}(CH_2)_m\text{-}C(OH)(Tr \text{ or } Im)\text{-}C \equiv C\text{-}CR_1R_2OPr \qquad (XII)$$

$$(X)_nPh\text{-}(CH_2)_m\text{-}C(OH)(Tr \text{ or } Im)\text{-}CR_4 = CR_3\text{-}CR_1R_2OZ \qquad (XIII)$$



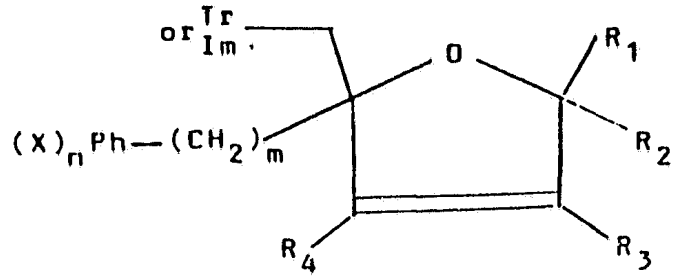
(XIV)



(XV)

The claims defining the invention are as follows:

1. A compound of the formula:



(I)

, in which

R_1, R_2, R_3 and R_4, which may be identical or different, each represents a hydrogen atom, or a lower alkyl, lower cycloalkyl, lower alkenyl, lower alkynyl or aryl radical, each such radical being optionally substituted, X represents a halogen atom, or an alkyl or alkoxy group containing from 1 to 12 carbon atoms, and optionally mono- or poly-halogenated or

X may also represent a cyano group,

n is zero or a positive integer which is less than 6, it being understood that when n is greater than 1, the substituents X may be identical or different,

Ph is an optionally substituted phenyl ring,

m = 0 or 1, and

Tr represents a 1,2,4-triazol-1-yl group and Im represents a 1,3-imidazol-1-yl group; and salts thereof and complexes thereof with metal salts.

2. A compound according to claim 1 wherein aryl radicals within the definition of R_1, R_2, R_3 and R_4 are

phenyl, substituted radicals within the definition of R_1, R_2, R_3 and R_4 are optionally substituted by one or more atoms or radicals selected from halogen atoms, lower alkoxy, aryloxy, aryl, lower alkyl, lower haloalkyl, lower haloalkoxy or hydroxy radicals and, within the definition of X the halogen atom is fluorine, chlorine or bromine and alkyl and alkoxy groups contain from 1 to 4 carbon atoms.

3. A compound according to claim 1 or 2 wherein m = 0.

4. A compound according to claim 1, 2 or 3 which contains a 1,2,4-triazol-1-yl group.

5. A compound according to any one of the preceding claims, wherein X represents a halogen atom and n = 1, 2 or 3.

6. A compound according to claim 5 wherein n is 1 or 2 and X is in the ortho and/or para positions.

7. A compound according to claim 5, wherein n = 2 and X is in the ortho and para positions.

8. A compound according to claim 5, 6 or 7 wherein X is chlorine.

9. A compound according to any one of the preceding claims, wherein R_1 and R_2 represent a hydrogen atom, and R_3 and R_4, which may be identical or different, each represents a lower alkyl radical, or one of R_3 and R_4 represents a lower alkyl radical, and the other represents a hydrogen atom.

10. A compound according to claim 1 hereinbefore identified as any one of compounds 1 to 15.

11. A process for the preparation of a compound according to claim 1, which comprises:

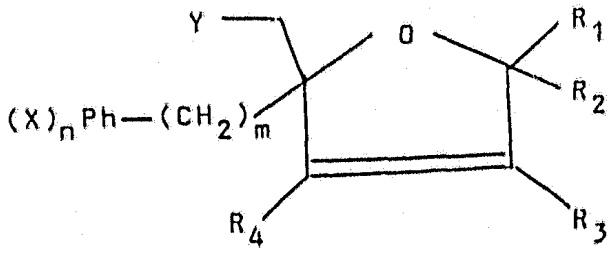
when R_3 and R_4 both represent a hydrogen atom, the hydrogenation of a compound of the formula:

$$(X)_n Ph-(CH_2)_m-C(OH)\ (CH_2Hal)-C\equiv C-CR_1R_2OPr \quad (IV)$$

in which X, n, Ph, m, R_1 and R_2 are as defined in claim 1, Pr represents a protective group, and Hal represents a halogen atom or, when one or each of R_3 and R_4 is other than a hydrogen atom, reaction of an organomagnesium compound of formula R_4MgX with a compound of formula IV and, if R_3 is other than hydrogen, addition of an alkyl halide of formula R_3X, cyclization of the compound thus obtained of the formula:

$$(X)_n Ph-(CH_2)_m-C(OH)(CH_2Hal)-CR_4=CR_3-CR_1R_2-OZ \quad (III)$$

in which R_1, R_2, R_3, R_4, X, Ph, n and m are as defined in claim 1, Hal is as hereinbefore defined, Z is a hydrogen atom or OZ is a leaving group, and the introduction of an imidazole or triazole ring into the compound thus obtained of the formula:



(II)

in which R_1, R_2, R_3, R_4, X, Ph, m and n are as defined in claim 1 and Y represents an atom or a group which can be removed by a nucleophilic substitution to introduce the imidazole or triazole ring, the groups OPr and Hal being converted if necessary, into groups OZ and Y respectively.

12. A process according to claim 11, wherein the hydrogenation is carried out using, as catalyst, palladium, ruthenium, Raney nickel, platinum or rhodium, deposited on an inert support.

13. A process according to claim 11 or 12, wherein the reaction with R_4MgX is carried out in the presence of copper iodide.

14. A process according to claim 11, 12 or 13, wherein when Y is a halogen atom, the compound of formula II is cyclized either in an acid medium if Z is a hydrogen atom, or in a basic medium if Z is a leaving group.

15. A process according to claim 14, wherein the cyclization reaction is carried out in the presence of 0.1 to 2 molar equivalents of acid per mol of compound of formula III.

16. A process according to claim 14, wherein the cyclization reaction is carried out in the presence of 0.01 to 2 molar equivalents of base per mol of compound of formula III.

17. A process according to claim 14, wherein the reaction temperature is from 10°C to 100°C, or, if a solvent

is present, at from 10°C to the reflux temperature of the reaction mixture.

18. A process according to any one of claims 11 to 14, which comprises treating with a base a compound of formula III in which Z is a hydrogen atom, R_1, R_2, R_3, R_4, X, Ph, m and n are as defined in claim 1 and Hal is as defined in claim 11, and optionally converting the hydroxy group Y in the compound of formula II thus obtained into a leaving group OZ.

19. A process according to claim 18 in which OZ represents a tosylate, mesylate, triflate or a group of formula $[Ph_3P^+-O-]$.

20. A process according to any one of claims 11 or 19, wherein the introduction of an imidazole or triazole group is carried out using an alkali metal, phosphonium or ammonium derivative of an imidazole or triazole, optionally formed in situ.

21. A process according to claim 20, wherein the molar ratio of the derivative relative to the compound of formula II is from 1.05 to 1.5.

22. A process according to any one of claims 11 to 21 wherein the introduction of an imidazole or triazole group is carried out in the presence of a solvent and wherein the quantity of compound of formula II relative to the total weight of the solution is from 1 to 70% by weight.

23. A process according to claim 22, wherein the

reaction temperature is near to the boiling point of the solvent.

24. A process for the preparation of a compound according to claim 1, which comprises:

reaction of a haloacetophenone of formula: $(X)_nPh(CH_2)_mCOCH_2Hal$ with an organometallic compound of formula: $R_2R_1C=CR_3-CHR_4M$ in which X, m, n, Ph, and R_1 to R_4 are as defined in claim 1, Hal is as defined in claim 11 and M represents an alkali metal, a magnesium-containing or a zinc-containing group to obtain a compound of the formual:

$$(X)_nPh-(CH_2)_m-C(OH)(CH_2Hal)-CHR_4-CR_3=CR_1R_2 \quad (V)$$

in which X, m, n, Ph and R_1 to R_4 are as defined in claim 1 and Hal is as defined in claim 11, introducing a triazole or imidazole ring into the compound of formula V to obtain a compound of the formula:

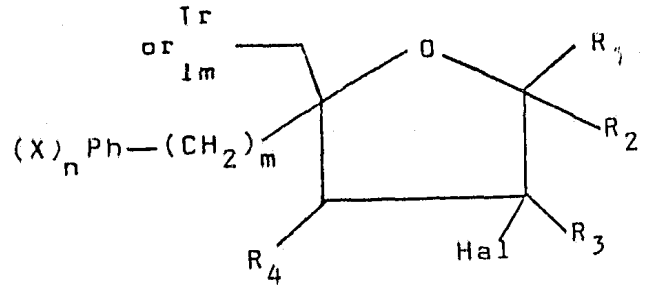
$$(X)_nPh-(CH_2)_m-C(OH)(Tr \text{ or } Im)-CHR_4-CR_3=CR_1R_2 \quad (VI)$$

in which X, m, n, Ph, R_1 to R_4, Im and Tr are as defined in claim 1, addition of a halogen or mixed halogen molecule to the compound or formula VI to obtain a compound of the formula:

$$(X)_nPh-(CH_2)_m-C(OH)(Tr \text{ or } Im)-CHR_4-CR_3Hal-CR_1R_2Hal \quad (VIII)$$

in which X, m, n, Ph, R_1 to R_4, Tr and Im are as

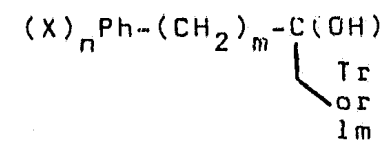
defined in claim 1 and Hal is as defined in claim 11, cyclization of the compound of formula VIII to obtain a compound of the formula:



(IX)

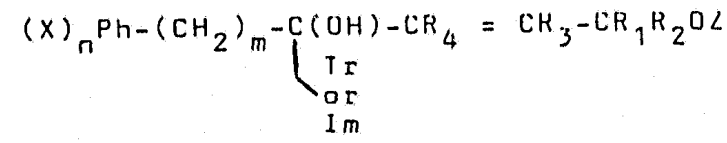
in which X, m, n, Ph, R_1 to R_4, Tr and Im are as defined in claim 1 and Hal is as defined in claim 11, and reacting the compound of formula IX with a base to obtain the compound of formula I.

25. A process for the preparation of a compound according to claim 1, which comprises introducing a triazole or imidazole ring into a compound of formula IV or III, depicted in claim 11, in which X, n, m, Ph and R_1 to R_4 are as defined in claim 1 and Hal, Pr and Z are as defined in claim 11 to obtain a compound of the formula:



(XII)

or



(XIII)

respectively, in which X, m, n, Ph, R_1 to R_4, Tr and Im are as defined in claim 1, and Pr and Z are as defined in claim 11, and then in hydrogenating, in the case of the compound of formula XII, and cyclizing to obtain the compound of formula I.

26. A process according to claim 25 in which the introductuon of a triazole or imidazole ring is carried out under the conditions defined in any one of claims 20 to 23, the hydrogenation is carried out under the conditions defined in claim 12 and the cyclisation is carried out under the conditions defined in any one of claims 14 to 19.

27. A process for the preparation of a compound according to claim 1 substantially as hereinbefore described.

28. A process for the preparation of a compound according to claim 1 substantially as hereinbefore described in any one of Examples 1 to 15.

29. A compound according to claim 1 when prepared by a process according to any one of claims 11 to 28.

30. A fungicidal composition which comprises, as active ingredient, a compound according to claim 1 or an agriculturally acceptable salt or complex thereof with a metal salt, in association with an agriculturally acceptable carrier.

31. A composition according to claim 30, which comprises from 0.5 to 95% by weight of active ingredient.

32. A composition according to claim 30 or 31 which comprises a surface active agent.

33. A composition according to claim 30 substantially as hereinbefore described in any one of Examples F1 to F9.

34. A method for the control of fungal diseases of crops at a locus which comprises the application thereto of a compound according to claim 1 or an agriculturally acceptable salt or complex thereof with a metal salt.

35. A method according to claim 34, wherein the active substance is applied at a rate of 0.005 to 5 kg/ha.

36. A method according to claim 35 wherein the rate is 0.01 to 0.5 kg/ha.

37. A method according to claim 34 substantially as hereinbefore described.

38. A compound of formula II, III or IV, in which X, n, m, Ph and R_1 to R_4 are as defined in claim 1 and Y, Z, Hal and Pr are as defined in claim 11.

39. The steps, features, compositions and compounds referred to or indicated in the specification and/or claims of this application, individually or collectively, and any and all combinations of any two or more of said steps or features.

Dated this 20th day of August 1987

RHONE-POULENC AGROCHIMIE
By its Patent Attorneys
DAVIES & COLLISON